Molecular dissection of adult liver regeneration to guide the generation of hepatocytes from pluripotent stem cells

Grant Award Details

Molecular dissection of adult liver regeneration to guide the generation of hepatocytes from pluripotent stem cells

Grant Type: New Faculty II

Grant Number: RN2-00950

Project Objective: to improve the differentiation and proliferation, and thus therapeutic efficacy of hepatocyte like cells (HLCs) derived from human pluripotent stem cells.

Investigator:

Name:	Holger Willenbring
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Liver Disease, Metabolic Disorders

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell

Award Value: $2,832,008

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Molecular dissection of adult liver regeneration to guide the generation of hepatocytes from pluripotent stem cells

Public Abstract: The liver is a promising target for cell therapy since it supports and functionally integrates transplanted cells. Human liver contains more than 50 billion cells and more than 10% replacement will be required for most liver diseases. Hence, embryonic stem cells (ESC), which have unlimited growth capacities, represent one of the few cell types with potential for liver cell therapy. However, to be functionally effective and safe, ESC have to be differentiated into hepatocytes, the cells of the liver that provide its typical functions, before transplantation. Unfortunately, current ESC differentiation protocols generate cells that are not fully differentiated or functional. To achieve levels of differentiation that would be therapeutic we propose to identify the mechanisms that establish hepatocyte function in progenitor cells in the adult liver. Adult liver progenitors are typically absent from the normal liver but become apparent in liver disease when hepatocytes are damaged. Remarkably, adult liver progenitors can differentiate into fully functional hepatocytes within a few days. We hope to identify the genes that enable this rapid maturation process in order to apply it to immature cells derived from ESC. If maturation can be induced and these hepatocyte-like cells function to correct a mouse model of a human liver disease we will have provided proof-of-principle for the potential of ESC for liver cell therapy.

Statement of Benefit to California: Liver transplantation is the only curative option for patients with severe liver diseases. As donor livers are rare, many Californians are currently waiting to receive a transplant. In fact, many patients on the waiting list die before a donor organ becomes available. If successful, the proposed project would help to alleviate the need for donor organs by establishing embryonic stem cells as a source of hepatocytes for transplantation. As hepatocyte transplantation would be less invasive and expensive than orthotopic liver transplantation, funds might become available that could be used to benefit the citizens of California in other areas.